REMARKS

Formal Matters

Claims 57-71 are now pending in this application.

The original claims along with newly added claims 21-56 have been canceled from the application and new claims 57-71 have been added to more particularly point out and distinctly claim the invention.

The newly added claims are believed to be fully supported within the originally filed application. New claim 57 is supported throughout the specification. Specific portions of the claims and support for such are pointed out here although other support within the application exists. For example, the general method as claimed in new claim 57 is supported in the summary of the invention on page 4. The concept of targeting an area of a patient's respiratory tract is supported at page 18, lines 25-27. Adjusting both the particle size and inhaled volume is supported at page 26, lines 15-23. The particle size ranges for targeting the specific area of the respiratory tract are supported at page 5, line 21 through page 6, line 5. The particle sizes are particle sizes of the particles having an aerodynamic diameter as described at page 19, line 20. The aerosol volume as well as the volume of free air inhaled prior to the aerosol and following the aerosol is supported at page 28, lines 3-10. The condensing agent and the particle size of the DNA after condensing is supported at page 10, lines 8-22 and specifically at lines 10 and 14.

New claims 58, 59, and 60 are supported respectively, within originally pending now canceled claim 2, 3 and 4 and in the specification at page 5, line 19 through page 6, line 5. New claims 61 and 62 are supported at page 41, line 10 through page 42, line 6 and claim 62 is specifically supported at page 41, lines 18, 19 and 24. New claims 63-69 are supported at page 10, lines 8-22, page 41, lines 1-9 and within the Examples beginning on page 49. New claims 70 and 71 are supported at page 29, lines 9-10. No new matter has been added.

Response in General

The previously pending 1-56 have been canceled and new claims 57-71 have been added to more particularly point out and distinctly claim the invention. The newly added claims are directed to a method of targeting an area of a patient's respiratory tract. This targeting is carried out by aerosolizing particles of polynucleotide and a condensing agent. The agent allows the polynucleotide to form particles which are present in the aerosolized particles and are quite small -- on the order of 20-50

nanometers. The polynucleotide particles are present in the aerosol particles which have their size adjusted within specific ranges depending on the area of the respiratory tract being targeted. Simultaneously the volume of aerosol inhaled is adjusted as is the volume of air inhaled prior to and after the aerosol is inhaled.

Thus, **three different factors** come into play in targeting the area of the lung.

First, the formulation includes the **polynucleotide and the condensing agent**. The condensed polynucleotide makes is possible to form particles which are more easily aerosolized to create the desired size for inhalation and targeting. Further, by condensing the polynucleotide they are less susceptible to enzymatic degradation as disclosed at page 10, line 13.

Second, the **size of the aerosol particles are adjusted** so that the particles more readily fit in the area of the lung being targeted. The larger particles will not reach to the alveoli and the much smaller particles will pass through the upper and middle areas of the airway.

Third, the **volume inhaled is controlled**. First by controlling the amount of free air inhaled prior to inhaling any aerosol, second by inhaling a predetermined volume of aerosolized particles and third by inhaling additional free air after the aerosol is inhaled (see an example at page 32, lines 10-24). It is preferably to also adjust the inspiratory flow rate as claimed in new claims 70 and 71. However, the basic concepts claimed in claim 57 of (1) adjusting aerosol particle size and (2) inhaled volume of an aerosolized (3) formulation comprised of a polynucleotide and condensing agent is not taught within the cited art as taken alone or in combination. Accordingly, reconsideration and withdrawal of the rejections is respectfully requested.

Claim 46 Withdrawn

Claim 46 was properly withdrawn as directed to the non-elected invention. All of the present claims are directed to a method of administering condensed polynucleotides and as such are directed to the elected invention.

Priority Claim

Applicants have noted the Examiner's position regarding the full scope of priority being afforded to the provisional application 60/089,146 filed on June 12, 1998.

Double Patenting Rejection

The double patenting rejection appears to now have been rendered moot by the cancellation of claims 51 and 52.

35 U.S.C. §112 Rejection

Previously pending claims were rejected under 35 U.S.C. §112, first paragraph and 35 U.S.C. §112, second paragraph. Without acquiescing to the validity of the rejection is it applicants' position that the objection has been rendered moot by the cancellation of these claims. Specific support for the method now claimed has been pointed out and the new claims are believed to be fully supported in the application and disclosed and described in a manner which would fully enable one of ordinary skill in the art. Accordingly, the rejection is believed to have been rendered moot.

35 U.S.C. §102 Rejection

Previously pending claims were rejected under 35 U.S.C. §102 as anticipated by Debs. The rejection is traversed as applied and as it might be applied to the presently pending claims. Debs does not disclose the basic concept of applicants' invention which involves **adjusting both the particle size of particles within an aerosol and volume inhaled in order to target a specific area of the respiratory tract**. By adjusting both the particle size and the inhaled volume in terms of the volume of aerosol as well as free air inhaled prior to and following the inhaled aerosol it is possible to specifically target areas of the respiratory tract with a formulation of polynucleotide and condensing agent. Such is not taught within the cited references as taken alone or in combination. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

35 U.S.C. §103 Rejections

Previously pending now canceled claims were rejected under 35 U.S.C. §103 over a combination of references. The rejections are traversed as applied and as they might be applied to the presently pending claims. Applicants do not claim to be the first to discover specific condensing agents or the first to discover that particle sizes must be within a general range in order to be inhaled into the lungs. However, the prior art does not teach adjusting the size of the particles of aerosol within a given range in order to target an area of the lung while also adjusting the inhaled volume of aerosol along with the inhaled volume of free air prior to the aerosol inhalation and after aerosol inhalation in order to target a particular area of the lung. Still further the art does not teach these concepts in combination with the use

of a condensing agent with a polynucleotide in order to create very small particles which are more readily formed into the aerosolized particles and which further allows the polynucleotide to be resistant to enzymatic degradation.

In deciding the question of obviousness under 35 U.S.C. §103 it is not realistic to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of the other parts necessary to the fully appreciation of what such a reference fairly suggests to one of ordinary skill in the art. Here, the taking of the disclosure from Debs relating to inhaling nucleotides and combining such with Schuster et al. which discloses adjusting the particle size is not realistic in that Debs is not teaching towards the adjustment of particle size in order to target areas of the lungs. The mere existence in the prior art of individual features of a claimed invention does not, without more, render the claimed invention obviousness within the meaning of 35 U.S.C. §103. There must be positive evidence that the bringing together of such features or steps would have been obvious to an ordinary skilled person. Here there is **nothing to suggest that the bringing together of all of the claimed steps would result in a method making it possible to specifically target areas of a patient's respiratory tract with aerosolized particles of a polynucleotide which has been condensed with a condensing agent**. In view of such reconsideration and withdrawal of the rejections is respectfully requested.

In the event that the Examiner find that minor issues remain unresolved the Examiner is respectfully requested to contact the undersigned attorney at the indicated telephone number to arrange for an interview to expedite disposition of this application.

In the event fees are due in connection with the filing of this document or the attached petition beyond those indicated on the petition the Commissioner is authorized to charge such fees to our Deposit Account 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: 30/NOV/2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please cancel claims 21-56 and add the following new claims 57-71.

57. (New) A method of targeting an area of a patient's respiratory tract, comprising:

delivering an aerosol to a patient while adjusting both particle size in the aerosol and volume inhaled;

wherein particle size is adjusted to an aerodynamic diameter related to a diameter of a targeted area of the respiratory tract within a range selected from the group consisting of:

(a) 1-3 μm to target alveoli of the respiratory tract;

(b) 4-6 μm to target central airways of the respiratory tract; and

(c) 7-10 μm to target upper airways of the respiratory tract; and

further wherein aerosol volume inhaled is controlled along with free air volume inhaled prior to and following inhalation of aerosol; and

still further wherein aerosol particles are comprised of a polynucleotide and a condensing agent which results in condensing polynucleotide particles to a size in a range of from about 20 to 50 nanometers, thereby delivering the particles of aerosol to a targeted area of the patient's respiratory tract.

58. (New) The method of claim 57, wherein the particle size is adjusted such that the aerodynamic diameter of the particles is in a range of from 1-3 μm.

59. (New) The method of claim 57, wherein the particle size is adjusted such that the aerodynamic diameter of the particles is in a range of from 4-6 μm.

60. (New) The method of claim 57, wherein the particle size is adjusted such that the aerodynamic diameter of the particles is in a range of from 7-10 μm.

61. (New) The method as claimed in claim 58, wherein the aerosol particles are further comprised of a cationic lipid.

62. (New) The method as claimed in claim 61, wherein the cationic lipid is selected from the

group consisting of DOTMA, DOTAP and DC-Chol.

63. (New) The method as claimed in claim 57, wherein the condensing agent is selected from the group consisting of protamine sulfate, polylysine, and combinations thereof.

64. (New) The method as claimed in claim 57, wherein the condensing agent is protamine sulfate.

65. (New) The method as claimed in claim 64, wherein the polynucleotide and protamine sulfate are present in a weight ratio of from about 2:1 to about 1:11.

66. (New) The method as claimed in claim 57, wherein the condensing agent is dextransulfate.

67. (New) The method as claimed in claim 57, wherein the condensing agent is a polyamine.

68. (New) The method as claimed in claim 67, wherein the polyamine is selected from the group consisting of spermine, spermidine and putrescine.

69. (New) The method as claimed in claim 57, wherein the condensing agent is selected from the group consisting of poly-lysine and poly-ethyleneimine.

70. (New) The method of claim 57, further comprising:

adjusting the patient's inspiratory flow rate inside a range of about 0.10 to about 4.0 liters/second.

71. (New) The method of claim 70, wherein the flow rate is adjusted inside a range of about 0.2 to about 3.0 liters per second.